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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/545,162	04/07/2000	ANTHONY P. SHUBER	EXT-026	1013

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EXAMINER	
SWITZER, JULIET CAROLINE	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 08/08/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/545,162	LAPIDUS ET AL.	
	Examiner	Art Unit	
	Juliet C. Switzer	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6/03* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is written in response applicant's correspondence submitted 4/28/03. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/28/03 has been entered.

2. The response filed 4/28/03 included a response to the final office action and a 1.132 declaration. Applicant's arguments and declaration have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. New rejections are set forth in this office action (Double Patenting).

4. Applicant's sequence listing and CRF filed 4/25/03 have been received and entered. The application is in compliance with the sequence rules.

5. The IDS filed 6/5/03 has been entered in to the application. A signed copy of the 1449 is enclosed with this office action.

Claim Rejections - 35 USC § 112

6. Claims 7-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods for screening a patient for colorectal cancer or precancer by determining in fecal matter a ratio between a first amount of long nucleic acid of a length greater than 200 base pairs and a second amount of nucleic acid of a length less than said long nucleic

acid, does not reasonably provide enablement for the detection of other types of cancer or precancer or the use of tissues or body fluids other than fecal matter or methods which do not specify the length of the nucleic acids which are detected. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claimed invention is drawn to encompass the identification of patients having any cancer or precancer by determining, in any body fluid or tissue comprising exfoliated cells, the presence of a fragment of nucleic acid that is "of a greater length than a length of said nucleic acid expected to be present in a sample from a healthy person" or whether an amount of DNA fragment greater than 200 base pairs exceeds a predetermined amount, wherein the DNA fragment is a degradation product of DNA that is present in both normal and precancerous cells or the ratio of long nucleic acids versus short nucleic acids. The specification demonstrates the method using a fecal matter sample for the screening of a patient for colorectal cancer or precancer by detecting the amount of three different long nucleic acid molecules (p53, K-ras, and apc). The specification demonstrates that for these three molecules PCR products of longer than 200 base pairs were present in the fecal matter of patients with colorectal cancer or precancer but such fragments were not present in healthy patients (Example 1). Neither the specification nor the prior art demonstrate that such a relationship exists for other cancers or for other body fluids or for lengths of less than 200 base pairs (as is encompassed by claim 7). The level of unpredictability for the detection of any disease using a nucleic acid assay is quite high. Since neither the specification nor the prior art provide any evidence of a universal association between a ration of nucleic acids greater than 200 base pairs to nucleic acids shorter than 200 base pairs

and every cancer and every body fluid, a practitioner wishing to practice the claimed invention would be required to provide the extensive experimentation necessary to demonstrate such an association. Such experimentation would in itself be inventive.

In light of the lack of guidance in the specification and the prior art, and in light of the high level of unpredictability in the instant subject matter, it is concluded that undue experimentation would be required to practice the instant invention commensurate in scope with the claimed invention.

It is noted that the claims that are present in allowed patent US 6143529 are of very similar scope to the instantly claimed invention. The instant rejection is not intended to call into question the validity of these claims because the claims in the '529 patent were allowed over a declaration.

Double Patenting

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 7-14 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 and 5 of copending Application No. 09/514865. Although the conflicting claims are not identical, they are not

patentably distinct from each other because the claims of the '865 application are an embodiment that falls within the instantly rejected claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

9. Claims 7-14 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-15 of U.S. Patent No. 6586177. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '177 patent are an embodiment that falls within the instantly rejected claims.

Response to Remarks

Applicant argues that the data in the declaration previously submitted in application 09/277016 support the contention that the specification of the instant application instant application enables claims 7-14. However, this is not persuasive. MPEP 2164.05 states that

> "To overcome a prima facie case of lack of enablement, applicant must demonstrate by argument and/or evidence that the disclosure, as filed, would have enabled the claimed invention for one skilled in the art at the time of filing. This does not preclude applicant from providing a declaration after the filing date which demonstrates that the claimed invention works. However, the examiner should carefully compare the steps, materials, and conditions used in the experiments of the declaration with those disclosed in the application to make sure that they are commensurate in scope; i.e., that the experiments used the guidance in the specification as filed and what was well known to one of skill in the art. Such a showing also must be commensurate with the scope of the claimed invention, i.e., must bear a reasonable correlation to the scope of the claimed invention."

The declaration under 37 CFR 1.132 filed 4/28/03 is insufficient to overcome the rejection of claim7-14 based upon scope of enablement as set forth in the last Office action because: First, the declaration does not argue or demonstrate that the INSTANT specification

was enabling at the time of the invention. The declaration does not discuss the instant specification, and in fact specifically states that the methodology used is similar to that used in Example 2 of 09/277016. This example is not repeated in the instant specification. Thus, while the specification demonstrates a method that can detect a variety of cancers (pancreas, lung, bile duct, esophageal, etc.) it is not sufficient to demonstrate that the methods set forth in the instant specification were enabled at the time the invention was made. Furthermore, the declaration does not address the breadth of claim 7, which encompasses identifying the presence of sequences even less than 200 bp in length. Thus, the scope of enablement rejection is maintained.

Further, it is noted that the declaration filed is not dated.

Conclusion

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C. Switzer whose telephone number is 703 306 5824. The examiner can normally be reached on Monday through Thursday, 9:00 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703 308 1119. The fax phone numbers for the organization where this application or proceeding is assigned are 703 305 3592 and (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308 0196.

Juliet C. Switzer
Patent Examiner
AU 1634

July 30, 2003

GARY BENZION, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600